



Approved for use through 07/31/2006. OMB 0651-0031

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Number	10/783,986
Filing Date	February 19, 2004
First Named Inventor	Ronit Satchi-Falnaró et al.
Art Unit	1614
Examiner Name	To be assigned
Attorney Docket Number	701039-52584-CIP

[illegible][illegible]

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



Substitute for form 1449 PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/783,986
				Filing Date	February 19, 2004
				First Named Inventor	Ronit Satchi-Fainaro et al.
				Art Unit	1614
				Examiner Name	To be assigned
Sheet	2	of	6	Attorney Docket Number	701039-52584-CIP

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
VB	C1	Folkman, J., Angiogenesis. in <i>Harrison's Textbook of Internal Medicine</i> (eds. Braunwald, E. et al.) 517-530 (McGraw Hill, New York, 2001).	
	C2	Hanahan, D. et al., Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis, <i>Cell</i> , 86:353-64 (1996).	
	C3	Volpert, O.V. et al., Id1 regulates angiogenesis through transcriptional repression of thrombospondin-1, <i>Cancer Cell</i> , 2:473-483 (2002).	
	C4	Folkman, J., Tumor angiogenesis, <i>Cancer Medicine</i> (eds. Holland, J. et al.), pp. 132-152 (B. C. Decker Inc., Ontario, Canada, 2000).	
	C5	Lyden, D. et al., Id1 and Id3 are required for neurogenesis, angiogenesis and vascularization of tumour xenografts, <i>Nature</i> , 401:670-677 (1999).	
	C6	Streit, M. et al., Thrombospondin-2: a potent endogenous inhibitor of tumor growth and angiogenesis, <i>Proc Natl. Acad. Sci. USA</i> , 96:14888-14893 (1999).	
	C7	Chin, L. et al., Essential role for oncogenic Ras in tumour maintenance, <i>Nature</i> , 400:468-472 (1999).	
	C8	Tabone, M.D. et al., Are basic fibroblast growth factor and vascular endothelial growth factor prognostic indicators in pediatric patients with malignant solid tumors?, <i>Clinical Cancer Res.</i> , 7:538-543 (2001).	
	C9	Yao, Y. et al., Prognostic value of vascular endothelial growth factor and its receptors Flt-1 and Flk-1 in astrocytic tumours, <i>Acta Neurochir (Wien)</i> , 143:159-66 (2001).	
VM	C10	Yuan, A. et al., Aberrant p53 expression correlates with expression of vascular endothelial growth factor mRNA and interleukin-8 mRNA and neoangiogenesis in non-small-cell lung cancer, <i>J. Clinical Oncology</i> , 20:900-910 (2002).	

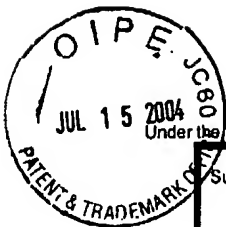
Examiner Signature	V. Balasubramaniam	Date Considered	9/30/04
-----------------------	--------------------	--------------------	---------

*EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



Substitute for form 1449 PTO			Complete if Known		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Application Number	10/783,986	
			Filing Date	February 19, 2004	
			First Named Inventor	Ronit Satchi-Fainaro et al.	
			Art Unit	1614	
			Examiner Name	To be assigned	
Sheet	3	of	6	Attorney Docket Number	701039-52584-CIP

✓	C11	Ingber, D. et al., Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumour growth, <i>Nature</i> , 348:555-557 (1990).	
	C12	Antoine, N. et al., AGM-1470, a potent angiogenesis inhibitor, prevents the entry of normal but not transformed endothelial cells into the G ₁ phase of the cell cycle, <i>Cancer Res.</i> , 54:2073-2076 (1994).	
	C13	Kudelka, A.P. et al., Complete remission of metastatic cervical cancer with the angiogenesis inhibitor TNP-470, <i>N. Engl. J. Med.</i> , 338:991-2 (1998).	
	C14	Kudelka, A.P. et al., A phase I study of TNP-470 administered to patients with advanced squamous cell cancer of the cervix, <i>Clinical Cancer Res.</i> , 3:1501-1505 (1997).	
	C15	Bhargava, P. et al., A Phase I and pharmacokinetic study of TNP-470 administered weekly to patients with advanced cancer, <i>Clinical Cancer Res.</i> , 5:1989-1995 (1999).	
	C16	Herbst, R.S. et al., Safety and pharmacokinetic effects of TNP-470, an angiogenesis inhibitor, combined with paclitaxel in patients with solid tumors: evidence for activity in non-small-cell lung cancer, <i>J. Clinical Oncol.</i> , 20:4440-4447 (2002).	
	C17	Kim, E.S. et al., Angiogenesis inhibitors in lung cancer. <i>Curr. Oncol. Rep.</i> , 4:325-333 (2002).	
	C18	Stadler, W.M. et al., Multi-institutional study of the angiogenesis inhibitor TNP-470 in metastatic renal carcinoma, <i>J. Clinical Oncol.</i> , 17:2541-2545 (1999).	
	C19	Logothetis, C.J. et al., Phase I trial of the angiogenesis inhibitor TNP-470 for progressive androgen-independent prostate cancer. <i>Clinical Cancer Res.</i> , 7:1198-1203 (2001).	
	C20	Rupnick, M.A. et al., Adipose tissue mass can be regulated through the vasculature, <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 99:10730-10735 (2002).	
✓	C21	Schoof, D.D. et al., The influence of angiogenesis inhibitor AGM-1470 on immune system status and tumor growth in vitro, <i>Int. J. Cancer</i> , 55:630-635 (1993).	

Examiner Signature	V. Balusubraman	Date Considered	9/30/04
--------------------	-----------------	-----------------	---------

*EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449 PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10783,986
				Filing Date	February 19, 2004
				First Named Inventor	Ronit Satchi-Fainaro et al.
				Art Unit	1614
				Examiner Name	To be assigned
Sheet	4	of	6	Attorney Docket Number	701039-52584-CIP

M	C22	Nagabuchi, E. et al., TNP-470 antiangiogenic therapy for advanced murine neuroblastoma, <i>J. Pediatric Surg.</i> , 32:287-93 (1997).	
	C23	Rihova, B. et al., Biocompatibility of N-(2-hydroxypropyl) methacrylamide copolymers containing adriamycin. Immunogenicity, and effect on haematopoietic stem cells in bone marrow in vivo and mouse splenocytes and human peripheral blood lymphocytes in vitro, <i>Biomaterials</i> , 10:335-342. (1989).	
	C24	Seymour, L.W. et al., The pharmacokinetics of polymer-bound adriamycin, <i>Biochem. Pharmacol.</i> , 39:1125-1131 (1990).	
	C25	Maeda, H. et al., Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review, <i>J. Controlled Release</i> , 65:271-284 (2000).	
	C26	Duncan, R. et al., Preclinical toxicology of a novel polymeric antitumour agent: HPMa copolymer-doxorubicin (PK1), <i>Human and Exp. Toxicology</i> , 17:93-104 (1998).	
	C27	Satchi-Fainaro, R., Targeting tumor vasculature: Reality or a dream?. <i>J. Drug Targeting</i> , 10:529-533 (2002).	
	C28	Duncan, R. et al., Polymers containing enzymatically degradable bonds, 7. Design of oligopeptide side chains in poly [N-(2-hydroxypropyl)methacrylamide] copolymers to promote efficient degradation by lysosomal enzymes, <i>Makromol. Chem.</i> , 184:1997-2008 (1983).	
	C29	Foekens, J.A. et al., Prognostic significance of cathepsins B and L in primary human breast cancer. <i>J. Clinical Oncol.</i> , 16:1013-1021 (1998).	
	C30	Gianasi, E. et al.. HPMa copolymer platinsates as novel antitumour agents: in vitro properties, pharmacokinetics and antitumour activity in vivo, <i>Eur. J. Cancer</i> , 35:994-1002 (1999).	
	C31	Kusaka, M. et al. Cytostatic inhibition of endothelial cell growth by the angiogenesis inhibitor TNP-470 (AGM-1470), <i>Br. J. Cancer</i> . 69:212-216 (1994).	
M	C32	Greene, A.K. et al., Endothelial-directed hepatic regeneration after partial hepatectomy, <i>Ann. Surg.</i> , 237:530-535 (2003)	

Examiner Signature	V. Balasubramanian	Date Considered	9/30/04
--------------------	--------------------	-----------------	---------

*EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449 PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/783,986
				Filing Date	February 19, 2004
				First Named Inventor	Ronit Satchi-Fainaro et al.
				Art Unit	1614
				Examiner Name	To be assigned
Sheet	5	of	6	Attorney Docket Number	701039-52584-CIP

M	C33	Drixler, T.A. et al., Liver regeneration is an angiogenesis- associated phenomenon, <i>Ann. Surg.</i> , 236:703-712 (2002).	
	C34	Klein, S.A. et al., Angiogenesis inhibitor TNP-470 inhibits murine cutaneous wound healing, <i>J. Surg. Res.</i> , 82:268-274 (1999).	
	C35	Whalen, C.T. et al., Assay of TNP-470 and its two major metabolites in human plasma by high-performance liquid chromatography-mass spectrometry, <i>J. Chromatographic Sci.</i> , 40:214-218 (2002).	
	C36	Brocchini, S. et al., Polymer-Drug conjugates: drug release from pendent linkers. in <i>Encyclopaedia of controlled release</i> (ed. Mathiovitz, E.) 786-816 (New York: Wiley, 1999).	
	C37	Duncan, R. et al., Polymer-drug conjugates, PDEPT and PELT: basic principles for design and transfer from the laboratory to clinic, <i>J. Controlled Release</i> , 74:135-146 (2001).	
	C38	Vasey, P.A. et al., Phase I clinical and pharmacokinetic study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: first member of a new class of chemotherapeutic agents-drug-polymer conjugates, Cancer Research Campaign Phase I/II Committee, <i>Clinical Cancer Res.</i> , 5:83-94 (1999).	
	C39	Seymour, L.W. et al., Tumour tropism and anti-cancer efficacy of polymer-based doxorubicin prodrugs in the treatment of subcutaneous murine B16F10 melanoma, <i>Br. J. Cancer</i> , 70:636-641 (1994).	
	C40	Dvorak, H.F. et al., Identification and characterization of the blood vessels of solid tumors that are leaky to circulating macromolecules. <i>Am. J. Pathology</i> , 133:95-109 (1988).	
	C41	Griffith, E.C. et al., Methionine aminopeptidase (type 2) is the common target for angiogenesis inhibitors AGM-1470 and ovalicin, <i>Chem. and Biol.</i> , 4, 461-471 (1997).	
	C42	Auerbach, R. et al., Angiogenesis assays: problems and pitfalls, <i>Cancer Metastasis Rev.</i> , 19:167-172 (2000).	
M	C43	Seymour, L.W. et al., Hepatic drug targeting: phase I evaluation of polymer-bound doxorubicin., <i>J. Clinical Oncol.</i> , 20:1668-1676 (2002).	

Examiner Signature	V. Balasubramanian	Date Considered	9/30/04
--------------------	--------------------	-----------------	---------

*EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449 PTO				Complete If Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/783,986
				Filing Date	February 19, 2004
				First Named Inventor	Ronit Satchi-Fainaro et al.
				Art Unit	1614
				Examiner Name	To be assigned
Sheet	6	of	6	Attorney Docket Number	701039-52584-CIP

W	C44	Francis, G.E. et al., PEG-modified proteins. in <i>Stability of Proteins Pharmaceuticals (Part B)</i> (ed. Ahem TJ, M.M.) 235-263 (Plenum Press, New York, 1992).	
	C45	Ho, D.H. et al., Clinical pharmacology of polyethylene glycol-L-asparaginase, <i>Drug Metabolism Disposition</i> , 14:349-352 (1986).	
	C46	O'Reilly, M.S. et al., Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma, <i>Cell</i> , 79:315-328 (1994).	
	C47	Folkman, J. et al., Long-term culture of capillary endothelial cells, <i>Proc. Natl. Acad. Sci. USA</i> , 76:5217-5221 (1979).	
	C48	Waynforth, H.B. Routes and methods of administration, Intracerebral injection. in <i>Experimental and Surgical technique in the rat</i> , Vol. 2.9 34-36 (Academic Press, London, 1980).	
	C49	Bhargava, P. et al., A Phase I and pharmacokinetic study of TNP-470 administered weekly to patients with advanced cancer, <i>Clinical Cancer Res.</i> , 5:1989-1995 (1999).	
	C50	Seymour, L.W. et al., The pharmacokinetics of polymer-bound adriamycin, <i>Biochemical Pharmacology</i> , 39:1125-1131 (1990).	
	C51	Yeh, J.R. et al., The antiangiogenic agent TNP-470 requires p53 and p21 ^{CIP/WAF} for endothelial cell growth arrest, <i>Proc. Natl. Acad. Sci. USA</i> , 97:12782-12787 (2000).	
	C52	Zhang, Y. et al., Cell cycle inhibition by the anti-angiogenic agent TNP-470 is mediated by p53 and p21 ^{WAF1/CIP1} , <i>Proc. Natl. Acad. Sci. USA</i> , 97:6427-6432 (2000).	
	C53	Seymour, L.W. et al., N-(2-hydroxypropyl) methacrylamide copolymers targeted to the hepatocyte galactose-receptor: pharmacokinetics in DBA ₂ mice, <i>Br. J. Cancer</i> , 63:859-866 (1991).	
M	C54	Folkman, J. Tumor angiogenesis. in <i>Accomplishments in cancer research</i> (eds. Wells, S.J. & Sharp, P.) 32-44 (Lippincott Williams & Wilkins, New York, 1998)	

Examiner Signature	V. Balasubram	Date Considered	9/30/04
--------------------	---------------	-----------------	---------

*EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.